Kidney International, Vol. 57, Suppl. 74 (2000), pp. S-94–S-99

Patient selection affects end-stage renal disease outcome comparisons

Francesco Locatelli, Daniele Marcelli, Ferruccio Conte, Lucia Del Vecchio, Aurelio Limido, Fabio Malberti, Donatella Spotti, and Sergio Sforzini, for the Registro Lombardo Dialisi e Trapianto[1]

Registro Lombardo Dialisi e Trapianto, Milano, Italy

Patient selection affects end-stage renal disease outcome comparisons. Geographic differences in dialysis patient outcome could be partially explained by demographic and baseline comorbid characteristics, including cardiovascular disease. To evaluate the influence of patient selection on outcome comparisons, we focus on the effect of cardiovascular disease on ESRD patient outcome using data from the Lombardy Registry. A total of 4139 ESRD patients (aged 61.9 ± 15.6 years, males 60.5%, diabetics 20%) who started renal replacement therapy (RRT) between 1994 and 1997 were considered. The analysis of 4-year survival in the presence or absence of ischemic heart disease and congestive heart failure at the beginning of RRT was performed using cardiovascular mortality and mortality from any cause as endpoints. Survival was compared by means of the Cox regression proportional hazard model; explanatory covariates were age, gender and diabetic status. Of the patients considered for the study, 918 (22.2%) died during the 4-year follow-up; the main cause of death was cardiovascular disease (cardiac causes in 304 patients [33.1%], vascular causes in 88 patients [9.6%.]). Patients with ischemic heart disease at the beginning of RRT had significantly higher mortality from myocardial infarction or from any cause than those without. The mortality risk for myocardial infarction was higher for elderly (RR = 1.04 per year; $P = 0.0001$) and diabetic patients (RR = 2.19; $P = 0.0006$). Chronic heart failure strongly affected overall mortality but not that from myocardial infarction. Ischemic heart disease and chronic heart failure are very common in incident ESRD patients and their presence is an important determinant of survival. Particular interventions are needed to prevent the development of cardiac abnormalities starting as early as possible during the predialytic phase.

The major clinical problems currently facing dialysis management are connected to the high level of morbidity and mortality. As in the case of many chronic medical conditions, the life expectancy of patients undergoing renal replacement therapy (RRT) is greatly reduced (20–25% that of the general population [1]). It is also well known that important geographic differences in end-stage renal disease (ESRD) survival exist, with US hemodialysis patients having a higher risk of death than those treated in Japan and in Europe [2]. However, registry data should be used with caution when comparing dialysis patient survival because they may be affected by several, sometimes hidden, factors. Indeed, country differences may include characteristics of the general population (life expectancy, prevalence of diabetes and cardiovascular diseases), the acceptance rate of uremic patients (the higher the acceptance rate, the higher the possibility of treating patients with several concomitant risk factors at the start of RRT), gender and age distribution, baseline comorbid conditions, withdrawal rate due to kidney transplant, and treatment modalities (hemodialysis/peritoneal dialysis) [3]. As the American National Cooperative Dialysis Study (NCDS) first demonstrated [4], patient morbidity and treatment failure were greatly related to inadequate dialysis doses. However, the consequent progressive increase in the mean dialytic dose and duration that has been obtained in the last decade in the United States seems to have only slightly reduced mortality [5]. This suggests that increasing age and a greater proportion of ESRD patients with complex medical comorbidity largely contribute to the lower survival in the United States. Age is certainly the most important demographic factor associated with increased mortality, together with the increasing incidence of ESRD diabetic patients. Malnutrition and anemia also contribute to higher mortality in RRT. The high prevalence of cardiovascular disease among dialysis patients is of particular concern, since this pathology accounts for more than 50% of mortality in these patients, at an approximately 30 times higher rate than in the general population [6]. The incidence of cardiovascular disease is not only high in diabetic primary hypertensive patients, but also among those with chronic glomerulonephritis, thus leading to the definition of chronic renal failure as a "vasculopathic state" [7].

[1] See Appendix for list of participating researchers and centers.

Key words: cardiovascular disease, congestive heart failure, dialysis.

The prevalence of the clinical manifestations of cardiovascular disease and echocardiographic abnormalities is already high at the beginning of RRT [8], and cardiac abnormalities are all independent predictors of both overall and cardiac mortality (more than two-thirds of dialysis patients with left ventricular hypertrophy [LVH] die from heart failure or sudden death [6, 9]). Furthermore, the long-term survival of hemodialysis patients experiencing acute myocardial infarction is disappointing when compared with that of the general population [10].

Given the detrimental impact of these complex comorbid conditions on dialysis patient quality of life and survival, their adequate assessment is extremely important not only in comparing outcomes in different dialysis populations, but also in possibly evaluating the effects of risk factor reduction and of other therapeutic interventions.

Aim of the present study was to assess the influence of patient selection on outcome comparisons, focusing on the magnitude of the effect of cardiovascular risk factors and of the presence of cardiac disease (i.e., ischemic heart disease and congestive heart failure [CHF]) at the beginning of RRT on ESRD patient outcome.

METHODS

Patients and data collection

The data used in this analysis came from the Dialysis and Transplant Lombardy Registry (RLDT), and included 4139 patients who started RRT for ESRD between January 1, 1994, and December 31, 1997 in the 44 Lombardy dialysis units. The Registry was begun in 1982 under the aegis of the Lombardy Regional Section of the Italian Society of Nephrology and the Regional Health Department. Data were collected at the end of each year (100% center response rate). A detailed study concerning the 1983–1992 dialysis and transplantation results in Lombardy has been published previously [11].

Patients having cardiovascular disease were defined as follows, according to the instructions of RLDT to dialysis centers: 1) coronary artery disease (CAD): clinical or instrumental evidence of coronary artery disease including coronary bypass, angioplasty; 2) myocardial infarction: documented myocardial infarction; 3) CHF: abnormality of cardiac function responsible for failure to pump at a rate commensurate with the requirements of the metabolizing tissues, by clinical or instrumental evaluation.

Statistical methods

The univariate descriptive analysis of survival were performed by the KaplanMeier technique, using mortality from myocardial infarction and mortality from any cause as end points. Evaluating general mortality, patients were censored when transferred to a dialysis unit out of Lombardy and at the final observation date (December 31, 1997). Evaluating mortality from myocardial infarction, the patient's death from any other cause were considered censors. In order to avoid the inclusion of "acute" patients, those patients who reached the end point or who were censored during the first 30 days of treatment, were excluded from the analysis. Thus, patient follow up ranged between 1 and 48 months.

Cox proportional hazard regression models [12] were used to evaluate the effect of the presence of ischemic heart disease and CHF on mortality from myocardial infarction and mortality from any cause, after having adjusted for age, gender and diabetic status. Ischemic heart disease at the beginning of RRT was defined as a single covariate with two levels of severity (i.e., CAD and myocardial infarction). The patients were censored as for the descriptive analysis.

All the statistical analyses were made using the SPSS version 7.5 (SPSS, Inc., Chicago, IL, USA) software package. The contribution of the covariates to explain the dependent variable was assessed by means of a two-tailed likelihood ratio test, with P-values < 0.05 being considered significant.

RESULTS

Patient characteristics

The mean age ($\pm$ SD) of the patients admitted to RRT was 61.9 $\pm$ 15.6 years, ranging from 60.1 $\pm$ 15.4 in 1994 to 62.5 $\pm$ 15.4 in 1997. There was an excess of male patients (males = 60.5%), which was without any significant change from 1994 to 1997. At the beginning of RRT, CAD and myocardial infarction were present in, respectively, 415 (10.0%) and 343 (8.3%) of the patients (total ischemic heart disease equal to 18.3%); CHF was present in 367 of the patients (8.9%). The percentage of incident ESRD patients with CAD or documented myocardial infarction at the beginning of RRT remained relatively stable during the four-year follow-up period (from 9.5% to 9.9% and from 8.4% to 8.6%, respectively), whereas the percentage of patients with CHF progressively increased (from 5.4 to 10.6%). The proportion of new patients with diabetes (both type 1 and type 2) as a comorbid risk factor was 20.0% (from 18% to 24%), whereas the percentage of new ESRD patients with diabetic nephropathy as primary renal disease was 11.9% in 1994 and increased to 17.1% in 1997.

Patient survival

Nine hundred eighteen (22.2%) patients died during the four-year period, with a death rate of 13.6 per 100 patient-years. Similarly to other Western countries, cardiovascular disease was the main cause of mortality, accounting for nearly 43% of the deaths (cardiac causes in 304 patients [33.1%] and vascular causes in 88 patients [9.6%]). Cachexia was the second cause of death (N =

Table 1. Relative risk rates for death from myocardial infarction by demographic and comorbid factors referring to the beginning of RRT according to Cox's main effect model

Covariate	RR	95% CI Lower	95% CI Upper	*P*
Age (per year)	1.04	1.02	1.06	0.0001
Gender (ref: F)	1.16	0.73	1.83	NS
Diabetes	2.19	1.4	3.42	0.0006
CHF	1.16	0.64	2.11	NS
CAD	2.88	1.63	5.08	0.0003
MI	5.94	3.55	9.95	<0.0001

Abbreviations are: CHF, congestive heart failure; CAD, coronary artery disease; MI, myocardial infarction.

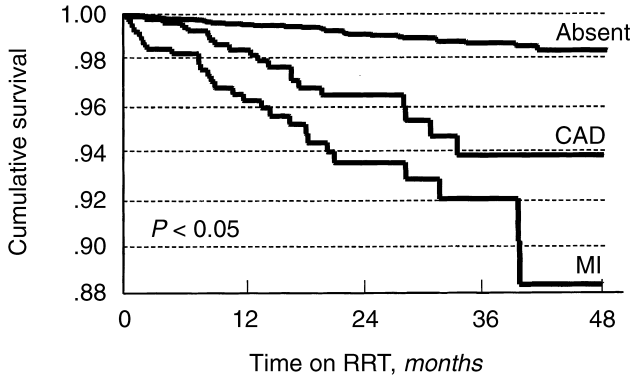

Fig. 1. Survival from myocardial infarction according to the presence of ischemic heart disease (CAD or myocardial infarction) at the beginning of RRT in the 1994–1997 incident ESRD patients of the Lombardy Registry, unadjusted.

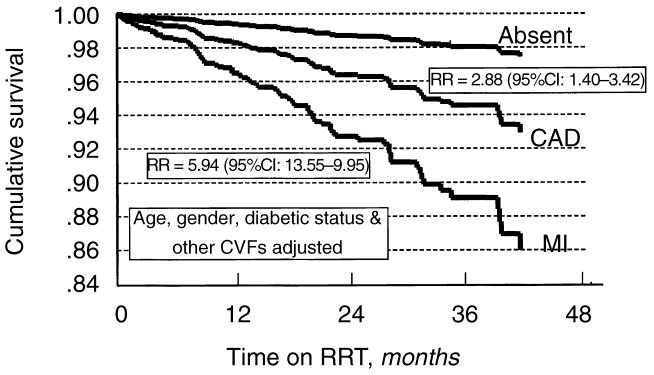

Fig. 2. Survival from myocardial infarction according to the presence of ischemic heart disease (CAD or myocardial infarction) at the beginning of RRT in the 1994–97 incident ESRD patients of the Lombardy Registry after adjusting for age, gender, diabetic status and other vascular diseases.

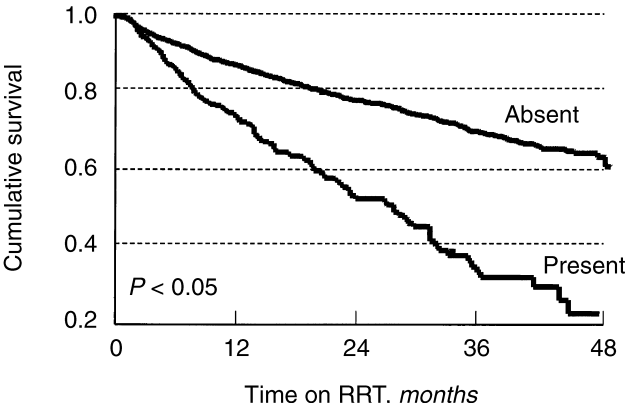

Fig. 3. Overall survival according to the presence of CHF at the beginning of RRT in the 1994–97 incident ESRD patients of the Lombardy Registry.

167, 18.2%), followed by malignancies ($N = 105$, 11.4%), infections ($N = 93$, 10.1%), gastrointestinal disease ($N = 42$, 4.6%), liver disease ($N = 14$, 1.5%) and social/psychological causes ($N = 12$, 1.3%). Miscellaneous causes accounted for the 10.1% of the deaths ($N = 93$).

The cumulative survival of all the ESRD patients was of 86.3%, 76.4% and 67.2% after 1, 2 and 3 years of follow-up, respectively.

The results based on the Cox proportional hazard model concerning mortality from myocardial infarction are given in Table 1. The mortality risk from myocardial infarction was higher for older patients (RR = 1.04 per year older; $P = 0.0001$). Compared with non-diabetics, the death rate from myocardial infarction of patients with diabetes as a comorbid condition was 2.19 higher ($P = 0.0006$). Gender did not significantly affect survival. As far as the role of ischemic heart disease is concerned, the results are presented in Figs. 1 and 2. Figure 1 shows a statistically significant higher mortality from myocardial infarction in patients with ischemic heart disease at the beginning of RRT, with a cumulative survival of about 98% after 48 months of follow-up in the absence of ischemic heart disease and of about 89% and 81%, respectively, in the presence of CAD or myocardial infarction. After adjusting for age, gender, diabetic status, and other vascular diseases, the relative death rate from myocardial infarction was still significantly higher in the presence of CAD (RR = 2.88, 95% confidence interval [1.40–3.42], $P = 0.0003$) or myocardial infarction (RR = 5.94, 95% confidence interval [3.55–9.95], $P < 0.001$) (Fig. 2).

The presence of CHF at the beginning of RRT did not influence mortality from myocardial infarction, but it strongly affected overall survival. The patients with this condition had markedly reduced 4-year survival that was significantly lower than that of the patients without (about 20% and 60%, respectively; $P < 0.05$) (Fig. 3). The adjusted death rate for the patients with CHF was 64% greater than that of the patients without (RR = 1.64, 95% confidence interval 1.36–1.98, $P < 0.0001$). Ischemic heart disease at the beginning of RRT also largely affected mortality from any cause. At 48 months,

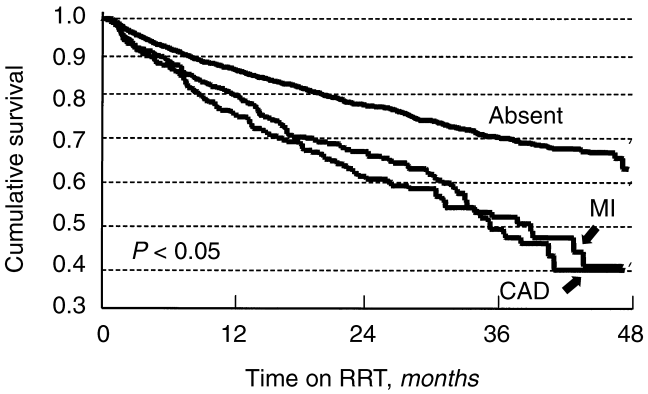

Fig. 4. Overall survival according to the presence of ischemic heart disease (CAD or myocardial infarction) at the beginning of RRT in the 1994–97 incident ESRD patients of the Lombardy Registry.

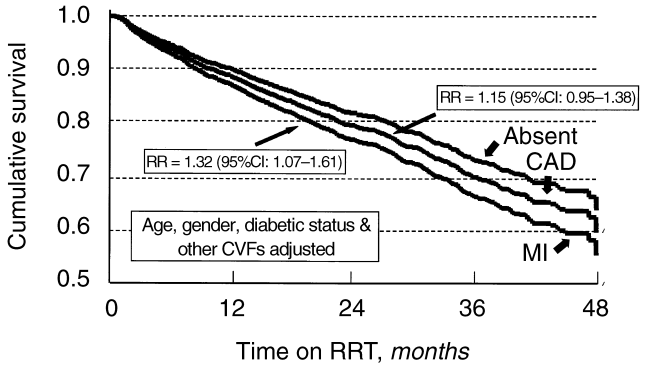

Fig. 5. Overall survival according to the presence of ischemic heart disease (CAD or myocardial infarction) at the beginning of RRT in the 1994–97 incident ESRD patients of the Lombardy Registry after adjusting for age, gender, diabetic status and other vascular diseases.

the patients with CAD or myocardial infarction had significantly lower survival (about 38% and 40%, respectively) compared with that of the patients without (about 65%) (Fig. 4). After adjusting for age, gender, diabetic status and other vascular diseases, mortality was still significantly higher in the presence of myocardial infarction at the beginning of RRT (RR = 1.32, 95% confidence interval 1.07–1.61) (Fig. 5). However, the adjusted death rate for the patients with CAD at the beginning of RRT was not statistically different from that of the patients without (RR = 1.15, 95% confidence interval 0.95–1.38). Table 2 shows the results based on the Cox proportional hazard model concerning mortality from any cause. Age, diabetic status, congestive heart failure and myocardial infarction all independently affected survival (RR of 1.06, 1.37, 1.64, 1.32, respectively), whereas CAD and gender did not.

Table 2. Relative risk rates for death from any cause by demographic and comorbid factors referring to the beginning of RRT according to Cox's main effect model

		95% CI		
Covariate	RR	Lower	Upper	*P*
Age (per year)	1.06	1.05	1.06	<0.0001
Gender (ref: F)	1.04	0.91	1.19	NS
Diabetes	1.37	1.18	1.59	<0.0001
CAD	1.15	0.95	1.38	NS
MI	1.32	1.07	1.61	0.009
CHF	1.64	1.36	1.98	<0.0001

Abbreviations are: CHF, congestive heart failure; CAD, coronary artery disease; MI, myocardial infarction

DISCUSSION

Cardiovascular disease is the major cause of death in ESRD patients. The excess risk for cardiovascular disease is partially due to a higher prevalence of conditions which are recognized as risk factors for cardiovascular disease in the general population, such as older age, hypertension, hyperlipidemia, diabetes, tobacco use, physical inactivity [6]. In addition, uremia itself provides a number of hemodynamic and metabolic perturbations that favor atheroma and clot formation and vascular-wall damage. Together with anemia, inadequate salt and water removal and consequent hypertension are also important determinants. For this reason, Kt/V has no longer been assumed to be the only means of estimating dialysis adequacy, and increasing importance has been given to treatment time in relation to an additional aspect of dialysis adequacy: achieving dry body weight and thus normalizing blood pressure. However, the awareness of the importance of dialysis adequacy has only partially improved survival in ESRD patients, who still have an extremely low life expectancy.

The results of our large epidemiological study confirm that cardiac disease is a very common condition in the incident ESRD patients at the beginning of RRT. This may be partially influenced by the fact that Lombardy has one of the highest acceptance rate of ESRD patients to RRT among European countries [11]. Indeed, higher acceptance rates increase the likelihood of treating patients with several concomitant risk factors that are more likely at risk of death. Increasing age and a greater proportion of ESRD patients with diabetes and complex medical comorbidity largely contribute to increased mortality. The elderly are frailer and intercurrent medical conditions are more likely to occur with advancing age. Furthermore, vascular disease and diabetes are the most frequent causes of ESRD in elderly patients, thus further increasing the risk of cardiovascular death.

Age of incident patients is continuously increasing in Lombardy: from 1994 to 1997 the proportion of patients older than 64 years increased from 44.6% to 53.5%. Selecting the patients without cardiovascular disease at the acceptance on dialysis treatment, the risk to develop *de novo* cardiovascular disease increases by 4% for each

year of age (RR = 1.04, 95% confidence interval 1.02–1.04, $P < 0.001$).

The proportion of ESRD patients affected by diabetes (considering not only the patients with diabetic nephropathy as primary renal disease, but all the patients with a diabetic status) who were accepted on dialysis in Lombardy from 1994 to 1997 also greatly increased (from 18.5% to 24.1%). It is well known that survival of ESRD diabetics is shorter than that of diabetics in the general population [13] and that of their nondiabetic ESRD counterparts, about half of the excess mortality being attributable to cardiovascular causes [14, 15]. As expected, in our population the diabetics without documented cardiovascular disease at baseline had a higher age-adjusted risk of developing cardiovascular disease thereafter (RR = 1.56, confidence interval 1.19–2.05, $P = 0.043$).

As in the general population, ischemic heart disease was an independent predictor of death from myocardial infarction in the dialysis patients of the Lombardy Registry. The relative risk of death due to this disease was higher when a myocardial infarction had already occurred than in the presence of only a certain degree of CAD or in the absence of cardiac disease. Perhaps patients who experienced an acute myocardial infarction had more severe coronary stenosis and thus were at increased risk of rapidly exhausting the coronary vasodilator reserve, even in the presence of minimal increases in myocardial oxygen requirement. However, the degree of atherosclerotic coronary arterial narrowing often does not predict the risk of thrombotic occlusion [16, 17].

Heart failure was not an independent predictor of cardiovascular death in our study. This is probably explained by the fact that CHF is caused by a number factors (such as volume overload, anemia, hypertension, arteriovenous fistula, uremia-related myocardial cell injury) besides ischemic heart disease that do not directly influence the development of CAD.

On the other hand, both symptomatic heart failure and ischemic heart disease negatively affected overall survival. However, CAD did not independently contributed to mortality. This is in agreement with the results of a Canadian multicenter study that prospectively followed a cohort of 433 ESRD patients for a mean of 41 months from the start of RRT [8]. In this study, cardiac failure at baseline was strongly predictive of overall mortality, whereas CAD and angina were without impact [18]. The role of CAD may be mediated by the development of cardiac failure and, as suggested by Parfrey et al [19], it may exerts its adverse impact through left ventricular pump dysfunction. In this process, LVH certainly plays a major role. In the presence of this condition, impairment of coronary perfusion may be catastrophic, resulting not only in regional impairment of left ventricular contraction but also in left ventricular dilation and systolic dysfunction [20]. On the other side around, it is likely that LVH predisposes to the development of ischemic symptoms [19]. Unfortunately, data were not available concerning the impact of LVH in our population.

It should be considered that the ability to maintain extracellular volume with ultrafiltration may obscure the diagnosis of CHF and hypotension either before or during the dialysis procedure may be the only manifestation of cardiac failure. Indeed, the already mentioned Canadian multicenter study found that low mean arterial blood pressure was independently associated with mortality (RR 1.36 per 10 mmHg fall, $P = 0.009$), probably reflecting the fact that cardiac failure occurred prior to death, as a consequence of cardiac hypertrophy or dilation [21]. Unfortunately, the Lombardy Registry is not able to collect data concerning interdialytic weight gains and blood pressure values. Thus, it is not possible to completely exclude either an overestimation of the prevalence of CHF because of fluid overload or, on the other side around, an underestimation in the patients in whom the presence of hypotension was the only symptom of CHF.

In conclusion, the results of our epidemiological study of a large number of dialysis patients confirm that cardiovascular disease is the main factor affecting morbidity and mortality. Particular interventions are therefore needed to prevent the development of cardiac abnormalities in this population. In particular, the correction of anemia, an adequate antihypertensive treatment, and the limitation of saline and volume overload are crucial. Given that patients starting RRT generally have such badly damaged hearts that they have reached not only ESRD but also "near-terminal cardiac failure" [22], these interventions should be started as early as possible in the predialytic phase. A more intensive approach to diagnosis and treatment of cardiovascular disease may also improve outcomes in ESRD patients [23].

APPENDIX: PARTICIPATING RESEARCHERS AND CENTERS

D. Marchesi and T. Bertani (Bergamo); P. Faranna (Trescore Balneario); G. Alongi and M. Lorenz (Zingonia); P. Ondei and L. Rusconi (Ponte S. Pietro); M. Massazza and M. Borghi (Treviglio); A. Strada and R. Maiorca (Brescia); S. Bove and F. Brandi (Brescia Umberto I): A. Testori (Desenzano); M. Brognoli and M. Usberti (Leno); R. Broccoli (Esine); F. Cossandi and S. De Marinis (Chiari); M. Fraticelli and R. Rossi (Como); B. Rivetti and F. Pecchini (Cremona); V. Ogliari and M. Mileti (Crema); G. Pontoriero, L. Del Vecchio and F. Locatelli (Lecco); F. Malberti and E. Imbasciati (Lodi); P. Botti and R. Tarchini (Mantova); A. Perego and G. Civati (Milano-Niguarda); G.C. Ambroso and C. Ponticelli (Milano-Croff); L. Luciani and G. D'Amico (Mi-

lano-S. Carlo); S. Bertoli and G. Barbiano di Belgioioso (Milano-Sacco); D. Spotti and G. Bianchi (Milano-San Raffaele); A. Baretta and D. Brancaccio (Milano-S. Paolo); A. Edefonti and F. Sereni (Milano-ICP); M: Beccari and G. Sorgato (Milano-FBF); M. Viganò and B. Redaelli (Monza); A. Manfredi and R. Marangoni (Bollate); F. Conte and A. Sessa (Vimercate); O. Bracchi and S. Sforzini (Cernusco SN); M. Saruggia and F. Vallino (Cinisello Balsamo); G. Bonforte and M. Surian (Desio); G. Renzetti and A. Colombo (Legnano); E. Orazi and C. Grassi (Melegnano); G. Pisano and C. Novi (Magenta); M. Doria and A. Frontini (S. Donato Milanese); A. Dal Canton (Pavia-S. Matteo); G. Villa and A. Salvadeo (Pavia-Cl. Lavoro); M. Nai and R. Bellazzi (Vigevano); W. Bazzini and C. Barbieri (Voghera); F. Samà and L. Pedrini (Sondrio); O. Amatruda and L. Gastaldi (Varese); A. Limido and P. Cantù (Gallarate); P. Scalia and C. Grossi (Tradate); and L. Brambilla Pisoni and A. Giangrande (Busto Arsizio).

Reprint requests to Prof. Dr. Francesco Locatelli, Department of Nephrology and Dialysis, Azienda Ospedale di Lecco, Via Ghislanzoni 22, 23900 Lecco, Italy.
E-mail: nefrolec@tin.it

REFERENCES

1. Eknoyan G: On the epidemic of cardiovascular disease in patients with chronic renal disease and progressive renal failure: a first step to improve the outcomes. *Am J Kidney Dis* 32(Suppl 3):S1–S4, 1998
2. Marcelli D, Stannard D, Conte F, Held PJ, Locatelli F, Port FK: ESRD patient mortality with adjustment for comorbid conditions in Lombardy (Italy) versus the United States. *Kidney Int* 50:1013–1018, 1996
3. Locatelli F, Marcelli D, Conte F: Dialysis patient outcomes in Europe vs the USA. Why do Europeans live longer? *Nephrol Dial Transplant* 12:1816–1819, 1997
4. Gotch FA, Sargent JA: A mechanistic analysis of the National Cooperative Dialysis Study (NCDS). *Kidney Int* 28:526–534, 1985
5. U.S. Renal Data System: USRDS 1998 Annual Data Report. *Am J Kidney Dis* 32(Suppl. 1):S69–S80, 1998
6. Levey AS, Beto JA, Coronado BE, Eknoyan G, Foley RN, Kasiske BL, Klag MJ, Mailloux LU, Manske CL, Meyer KB, Parfrey PS, Pfeffer MA, Wenger NK, Wilson PW, Wright JT Jr: Controlling the epidemic of cardiovascular disease in chronic renal disease: what do we know? What do we need to learn? Where do we go from here? National Kidney Foundation Task Force on Cardiovascular Disease. *Am J Kidney Dis* 32(5):853–906, 1998
7. Luke RG: Chronic renal failure—A vasculopathic state. *N Engl J Med* 339:841–843, 1998
8. Foley RN, Parfrey PS, Harnett JD, Kent Gm Martin CJ, Murray DC, Barre PE: Clinical and echocardiographic disease in patients starting end-stage renal disease therapy. *Kidney Int* 47:186–192, 1995
9. Silberberg JS, Barre PE, Prichard SS, Sniderman AD: Impact of left ventricular hypertrophy on survival in end-stage renal disease. *Kidney Int* 36:286–290, 1989
10. Herzog CA, Ma JZ, Collins AJ: Poor long-term survival after acute myocardial infarction among patients on long-term dialysis. *N Engl J Med* 339:799–805, 1998
11. Locatelli F, Marcelli D, Conte F, Limido A, Lonati F, Malberti F, Spotti D: 1983–92: Report on regular dialysis and transplantation in Lombardy. *Am J Kidney Dis* 25:196–205, 1995
12. Cox DR: Regression models and life tables (with discussion). *J R Statist Soc* 34:197–200, 1972
13. Sarnak MJ, Levey AS: Epidemiology of cardiac disease in dialysis patients. *Semin Dial* 12:69–76, 1999
14. Marcelli D, Spotti D, Conte F, Tagliaferro A, Limido A, Lonati F, Malberti F, Locatelli F: Survival of diabetics patients on peritoneal dialysis or hemodialysis. *Perit Dial Int* 16(Suppl. 1):S283–S287, 1996
15. Byrne C, Vernon P, Cohen JJ: Effect of age and diagnosis on survival of older patients beginning chronic dialysis. *JAMA* 271:34–36, 1994
16. Ambrose J, Tannenbaum M, Alexopoulos D, Hjemdahl-Monsen CE, Leavy J, Weiss M, Borrico S, Gorlin R, Fuster V: Angiographic progression of coronary artery disease and the development of myocardial infarction. *J Am Coll Cardiol* 12:56–62, 1988
17. Little W, Constantinesco M, Applegate RJ, Kutcher MA, Burrows MT, Kahl FR, Sanatamore WP: Can coronary angiography predict the site of a subsequent myocardial infarction in patients with mild-to-moderate coronary artery disease? *Circulation* 78: 1157–1166, 1988
18. Parfrey PS, Griffiths SM, Harnett JD, Taylor R, King A, Hand J, Barre PE: Outcome of congestive heart failure, dilated cardiomyopathy, hypertrophic hyperkinetic disease, and ischemic heart disease in dialysis patients. *Am J Nephrol* 10(3):213–221, 1990
19. Parfrey PS, Foley RN, Harnett JD, Kent GM, Murray D, Barre PE: Outcome and risk factors for ischemic heart disease in chronic uremia. *Kidney Int* 49:1428–1434, 1996
20. Parfrey PS, Foley RN, Harnett JD, Kent GM, Murray D, Barre PE: The outcome and risk factors for left ventricular disorders in chronic uremia. *Nephrol Dial Transplant* 11:1277–1285, 1996
21. Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC, Barre P: Impact of hypertension on cardiomyopathy, morbidity and mortality in end-stage renal disease. *Kidney Int* 49:1379–1385, 1996
22. Silverberg D, Blum M, Peer G, Iaina A: Anemia during the predialysis period: a key to cardiac damage in renal failure. *Nephron* 80:1–5, 1998
23. Delemos JA, Hillis JD: Diagnosis and management of coronary artery disease in patients with end-stage renal disease on hemodialysis. *J Am Soc Nephrol* 7:2044–2054, 1996